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PATENT APPLICATION
Docket No.:0725.1056-001(formerly HU98-02PA)

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	James M. Hogle, Harmon J. Zuccola, David Filman and Carl Elkin		
Application No.:	09/347,175	Group Art Unit:	1645
Filed:	July 1, 1999	Examiner:	R. Zeman

For: OLIGOMERIZATION OF HEPATITIS DELTA ANTIGEN

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231

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PETITION UNDER 37 C.F.R. 1.144

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This is a Petition to the Restriction Requirement made final in Paper No. 14, mailed October 22, 2001. Group I has been elected and examined. This petition is supported by the traversals presented in the Reply to Restriction Requirement dated August 8, 2001 and the Amendment dated January 10, 2002. This Petition is timely under 37 C.F.R. 1.144. Withdrawal of the restriction is requested.

The Invention

The invention relates to the discovery that a specified fragment of HDAg forms an antiparallel coiled coil with hydrophobic residues near the termini of each peptide forming an extensive hydrophobic core with residues C-terminal to the coiled coil domain in a dimer protein. The dimers associate further to form highly organized octamers through residues in the coiled coil domain. See Figure 5. The octamers serve as a convenient high valency framework for linking a variety of functional peptides and domains, e.g., via preparation of fusion proteins comprising the HDAg fragment and the functional peptide or domain (e.g., a binding moiety). Thus, the invention relates, inter alia, to the monomer (e.g., a fusion protein comprising the HDAg fragment and a binding moiety), coiled coil dimers thereof and octamers thereof.

Criteria for Restriction

There are two criteria for a proper requirement for restriction between patentably distinct inventions: (a) the inventions must be independent or distinct as claimed; and (b) there must be a serious burden on the examiner if restriction is required. (Manual of Patent Examining Procedure MPEP, 8th edition, 803).

The Restriction Requirement

The restriction requirement sets forth 52 different groups for restriction. Because of the complexity of the restriction requirement, the traversal has been limited to the particular Groups for which recombination is requested.

Applicants respectfully requests that certain groups be recombined with elected Group I. Specifically, Applicants requests that Groups I, II, XXVI-XLVII and XLVIII be combined and examined together. These Groups were selected because of their closely related subject matter. The Groups of interest, the claims encompassed by the Groups, and the subject matter of the Groups are set forth in the following Table.

Group Number	Claims in Group	Restriction requirement description of Subject Matter of Claims in Group
I	1-6	Fusion molecules comprising an HDAg fragment coil and at least 1 binding moiety, classified in class 424, subclass 225.1.
II	7-10, 18 and 19	A coiled-coiled oligomer comprising the fusion molecules, classified in class 530, subclass 350.
XXVI-XXXI	16 and 20	A polypeptide encoded by SEQ ID NO: 10 (Group XXVI); SEQ ID NO: 12 (Group XXVII);SEQ ID NO: 13 (Group XXVIII); SEQ ID NO: 14 (Group XXIX); SEQ ID NO: 21 (Group XXX); SEQ ID NO: 23 (Group XXXI). Classified in class 530, subclass 350.
XXXII-XLVII	17 and 21	A polypeptide encoded by SEQ ID NO: 1 (Group XXXII); SEQ ID NO: 2 (Group XXXIII);SEQ ID NO: 3 (Group XXXIV); SEQ ID NO: 4 (Group XXXV); SEQ ID NO: 5 (Group XXXVI); SEQ ID NO: 6 (Group XXXVII).... Classified in class 530, subclass 350.

XLVIII	41-45	Methods of enhancing the interaction between binding partners. Classified in class 435, subclass 7.1.

Modification of the restriction requirement to consider these Groups concurrently is appropriate for the reasons set forth below.

A. Groups I and II should be rejoined

1. Claims 1 and 7-10 are a combination/subcombination which lacks two-way distinctness

The Examiner states at page 8 of the Office Action that inventions I, II and XXVI-XLVII are separate and distinct from each other as they comprise completely differing biochemical and physical entities having differing properties and uses. Applicants respectfully disagree.

Elected Group I consists of Claims 1-6. Claim 1 is directed to a fusion molecule consisting essentially of the specified HDAg fragment coil and at least one binding moiety. Claims 7-10 are in Group II. Claim 7 is directed to a coiled-coil oligomer comprising at least two fusion molecules of Claim 1, and Claims 8-10 are dependent upon Claim 7, providing further limitations on the oligomer. That is, Claim 7 is directed to a composition containing at least two molecules of Claim 1, in a specified organizational relationship (i.e., a coiled-coil) and is a "combination" of two molecules of Claim 1. Therefore, Claim 1 is a subcombination of the combination of Claims 7-10. See M.P.E.P. §806.05(a) ("A combination is an organization of which a subcombination or element is a part").

To support a requirement for restriction, two-way distinctness must be demonstrated. M.P.E.P 806.05(c). To establish distinctness, it must be shown that the combination as claimed does not require the particulars of the subcombination as claimed for patentability. Here, Claims 7-10 do require the particulars of Claim 1 as the essential distinguishing feature of the Claims, and, thus, the inventions are not distinct. As set forth in MPEP 806.05(c)(II), "If there is no evidence that combination ABsp is patentable without the details of Bsp, restriction should not be required." Here, A=Bsp=the fusion protein of Claim 1. Claim 7 requires the details of Claim

1 and is, thus, patentable with the details of Claim 1. Therefore, the requirement for restriction should not be made.

Furthermore, the Examiner has failed to show any burden in searching these two groups. The restriction requirement misstates the classification of Group I. Claim 1, drawn to a fusion protein, not a pharmaceutical composition or method of use, has an original classification within Class 530, like Group II, not Class 424. Both groups enjoy the same classification as compositions containing peptide oligomers. Claim 7, a multimer or dimer of Claim 1, with a specified physical orientation, enjoys the same classification. Further the search of a composition containing a dimer, or other oligomer, of the fusion proteins of Claim 1 will necessarily include the search of the monomer. Thus, no burden is found in searching these claims together in a single application.

The Examiner does not address any of these specific arguments specifically but generally maintains the restriction.

2. The peptide of Claim 18 differs from HDAg of Claim 1 solely by a single residue

Although Claim 18 has been placed in Group II, it is not drawn to a coiled-coiled oligomer comprising fusion molecules. Rather, Claim 18 is directed to a derivative of an HDAg peptide wherein a serine residue is substituted with a single residue, cysteine. As such, the classification of the two groups should be the same. In view of the close similarity between the two core sequences, the literature and electronic searches should also be the same. Since the search for Group I would include art related to HDAg, the substitution of a single amino acid will not seriously increase the search burden for the Examiner. Under the decision of *In re Weber*, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 198 USPQ 334 (CCPA 1978), it is improper for the Patent Office to refuse to examine that which applicants regard as their invention unless it lacks unity of invention. MPEP 803.02. Unity of invention exists where the compounds share a common utility and a substantial structural relationship, disclosed as being essential to that utility. In this case, the sequences of Claims 1 and 18 both form coiled coil oligomers, due to their substantial structural relationship. No burden in searching these two closely related sequences has been offered by the Examiner other than the general assertion that each and every

product of matter is to be claimed in a separate application. However, such a position is clearly untenable in view of the statutes and caselaw which explicitly provide the right of Applicants to examine multiple embodiments of an invention in a single patent application.

B. Groups I and XXVI-XLVII should be rejoined

1. Claims 16, 17, 20 and 21 are each directed to compounds within Markush groups with common utility and a common structural feature responsible for the utility

The Restriction Requirement includes five groups, XXVI-XXXI, which each contain the same two claims, Claims 16 and 20. These claims are both dependent upon Claim 11, which contains a Markush group directed to nucleic acid molecules. Claims 16 and 20 are restricted into the five groups based on the SEQ ID NOs. of the nucleic acid molecules in the Markush group.

Likewise, the Restriction Requirement includes 11 groups, XXXII-XLVII, which each contain the same two claims, Claims 17 and 21. Claim 17 is directed to a molecule comprising a polypeptide having an amino acid sequence selected from a Markush group comprising amino acid sequences identified by SEQ ID NO's., portions of such sequences, and fragments and derivatives thereof which form a coiled-coil oligomer. Claim 21 is ultimately dependent upon Claim 12, which contains a same Markush group comprising the same amino acid sequence identified by SEQ ID NO's as Claim 17. Claims 17 and 21 are restricted into the 11 separate groups based on these SEQ ID NO's.

These restrictions are both improper unless it can be shown that the subject matter of the claims lacks a common utility and a common structural feature responsible for the utility.

Since the decisions *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which Applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where

compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility. (MPEP § 803.02).

The compounds of Groups XXVI-XXXI all share a common utility, namely, they all encode a polypeptide which forms a coiled-coil oligomer. They also share a common structural feature responsible for that activity, i.e., they comprise nucleic acid sequences which encode these polypeptides. Therefore, these groups should be rejoined.

Likewise, the compounds of Groups XXXII-XLVII all share a common utility, namely, they all form a coiled-coil oligomer. They also share a common structural feature responsible for that activity, i.e., they comprise the amino acid sequences which form a coiled-coil oligomer. Therefore, these groups should be rejoined.

When these two criteria (common utility and structural feature) are satisfied, MPEP §803.02 provides a procedure for examining the entire scope of the claim containing the Markush group. Specifically, there is a requirement for an election of species, followed by an examination of the entire scope of the elected species and further to the extent necessary to determine patentability of the Markush-type claim:

> In applications containing claims of that nature, the examiner may require a provisional election of a single species prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration. (Emphasis added).

Applicants therefore request that both restriction requirements be withdrawn and replaced with requirements for election of species (i.e., SEQ ID NOS.). Applicants request further that the elected species be examined, and, upon a finding that the elected species is allowable, that the entire scope of the claims be examined. In the event that the restriction requirement is replaced with a requirement for election of species, Applicants hereby elect the peptide encoded by SEQ ID NO: 10.

Furthermore, Applicants traverses the Examiner's requirement based on the clear statement in MPEP § 803.04, and in the Official Gazette Notice dated November 19, 1996, regarding the examination of patent applications containing nucleotide sequences, which state that "...the Commissioner has decided *sua sponte* to partially waive the

requirements of 37 C.F.R. § 1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application. Accordingly, in most cases, up to ten (10) independent and distinct nucleotide sequences will be examined in a single application without restriction." In accordance with these established guidelines, Applicant submits that it is reasonable to examine up to approximately ten nucleotide sequences in the subject application, and that, therefore, the six sequences in Groups XXVI-XXXI can be recombined, and, the 11 sequences in Groups XXXII-XLVII can be recombined.

Moreover, as stated in the MPEP at §808.02, in relevant part:

> Where, however, the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, no reasons exist for dividing among related inventions.

Here, the claims in Groups XXVI-XLVII have been placed in the identical class and subclass, class 530, subclass 350, and as stated by the Examiner, are related as products. Contrary to the requirements for imposing a restriction requirement when claims are so classified, no evidence has been offered to clearly indicate that the claimed inventions have acquired a separate status in the art, nor has any evidence been presented to show that any of the inventions of Groups XXVI-XLVII would necessitate a search in an area where no art pertinent to the other Groups exists.

The Examiner maintains the restriction requirement stating that "Office policy" is to permit only a single species to be examined in a single application. It is further stated that, since each species may differ in biochemical and physical properties, the search is not coextensive in scope. It is noted that the courts and statutes do not contemplate defining the burden of search to justify a restriction requirement as being a requirement that the search be "coextensive in scope." Certainly, that was not the case in *Weber* and *Haas*. That is certainly not the test applied in MPEP 803.02 which clearly contemplates the examination of structurally related (not identical) species which do not share a coextensive search. Likewise identity in physical and biochemical properties is also not required by this jurisprudence to present claims drawn to multiple embodiments in a single application.. Thus, if the Examiner's representation of Office "policy" is accurate, it is clearly not well founded in the law. Reversal is requested.

2. Claims 16 and 17 relate to Claim 1 as a combination/subcombination

Like Claim 19 in Group II, Claims 16 and 17 are each drawn to peptides comprising amino acid sequences of HDAg. Such peptides are a subcombination of the fusion molecule of Claim 1, which comprises HDAg and at least one binding moiety. The claims lack two-way distinctness because Claim 1 requires the particulars of HDAg as an essential distinguishing feature. Therefore, restriction of the claims into separate groups is improper.

3. No serious burden if Claims 20 and 21 are rejoined with Claim 1

Claims 20 and 21 are drawn to peptides encoded by fusion genes comprising HDAg nucleic acid molecules and heterologous (non-HDAg) peptides. The claims are related, because HDAg of Claim 1 can be encoded by the nucleic acid molecules, the binding moiety of Claim 1 can be heterologous peptide, and, likewise, the heterologous peptide can be a binding moiety. For Claims 20 and 21, as well as Claim 1, the Examiner would search for art regarding HDAg bound to another entity, specifically, a binding moiety (which can be a heterologous peptide) or a heterologous peptide (which can be a binding moiety). Therefore, a single search will identify relevant art pertaining to HDAg and the moiety and/or peptide, so recombining these groups would not be unduly burdensome. Therefore, restriction is not required for these claims.

C. Request for rejoinder of Group XLVIII (Claims 41-45) to Group I (Claims 1-6) is requested under 35 U.S.C. §103(b)

The Examiner states that the inventions I, II and XXVI-XLVII are related to the inventions XLVIII-LII as product and process of use, but are distinct because the compounds of I, II and XXVI-XLVII can be used in other methods such as immunization and antibody production. However, under 35 U.S.C. §103(b)(1), upon timely election by a patent applicant, a biotechnological process using a composition of matter that is novel and nonobvious is considered nonobvious if claims directed to the process and claims directed to the composition are contained in the same application and are owned by the same person. Under §103(b)(2), a patent issued on the process shall also contain the claims to the composition used in that process.

Rejoinder of Group XLVIII (Claims 41-45) and elected Group I (Claims 1-6) is requested because Claims 41-45 recite a biotechnological process using the molecule of Claim 1 and the claims are in the same application and owned by the same entity. Therefore, under §103(b)(2), they should be rejoined.

The Examiner asserts "enhancing binding interactions" is not a "biotechnological process." See Paper No. 16, page 2. However, the claim is clearly a method of using the product of Claim 1. Methods of use are biotechnological processes, irrespective of whether or not the preamble employs that literal language. Thus, the Examiner again fails to specifically address the grounds for the traversal.

CONCLUSION

Based on the above arguments, Applicants respectfully requests that the Restriction Requirement be modified as presented herein. Reconsideration and modification of the restriction requirement is requested.

If the Examiner believes that a telephone conversation would expedite prosecution of the application, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

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